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DOCKET NO.: ISIS-1158 **PATENT**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: **Nielsen, *et al.*** Confirmation No.: **8648**

Serial No.: **08/319,411** Group Art Unit: 1631

Filing Date: **October 6, 1994** Examiner: **Ardin H. Marschel**

For: **Peptide Nucleic Acid Conjugates**

EXPRESS MAIL LABEL NO: EV 631246708 US
DATE OF DEPOSIT: October 4, 2005

Mail Stop Appeal-Brief Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

APPELLANT'S BRIEF PURSUANT TO 37 C.F.R. § 41.37

This brief is being filed in support of Appellants' appeal from the rejections of claims 53, 63, And 64 dated October 6, 2004. A Notice of Appeal was filed on April 5, 2005.

1. REAL PARTY IN INTEREST

Based on information supplied by Applicants and to the best of the undersigned's knowledge, the real parties in interest in the above-identified patent application are Peter Nielsen, who is the assignee of Soren Holst Sonnichsen and Jesper Lohse; Ole Buchardt; Michael Egholm; Rolf Henrik Berg, and ISIS Pharmaceuticals, Inc., a corporation of Delaware.

2. RELATED APPEALS AND INTERFERENCES

There are no other appeals or interferences known to Appellants, Appellants' legal representative, or the assignee which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending Appeal. Applicants note, however, that prosecution was suspended in copending application 08/817,067 on October 1, 2002 due to a potential interference.

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3. STATUS OF CLAIMS

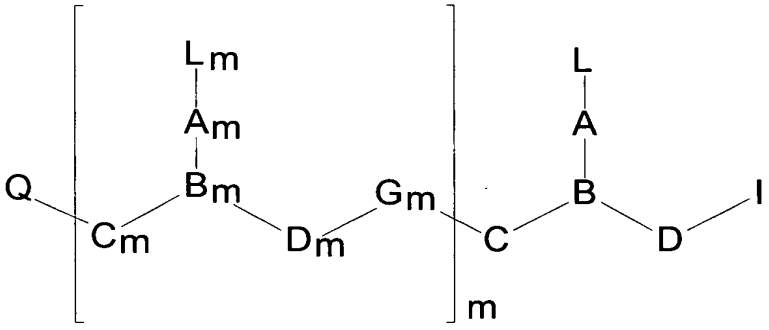
Claims 53, 63, and 64 are pending and are rejected for allegedly being unpatentable under the judicially created doctrine of obviousness-type double patenting over claims 1, 4, 5, and 7 of U.S. Patent No. 6,395,474 ("the 474 patent") and over claims 1 and 12 of U.S. Patent No. 6,613,873 ("the 873 patent"). The September 19, 2005 Advisory Action indicates that the rejection over claim 1 of U.S. Patent No. 5,773,571 has been overcome. The rejection of claims 53, 63, and 64 based on U.S. Patent No. 6,613,873 is appealed. Applicants have expressed a willingness to file a terminal disclaimer to remove the rejection based on U.S. Patent No. 6,395,474 once the claims otherwise are indicated as allowable.

4. STATUS OF AMENDMENTS

All amendments are believed to have been entered. A complete listing of currently pending claims is provided in the Claims Appendix.

5. SUMMARY OF CLAIMED SUBJECT MATTER

The claims are directed to peptide nucleic acids having the formula:



where m is an integer from 1 to about 50; L and L_m independently are naturally occurring nucleobases; C and C_m are $(CR^6R^7)_y$; R^6 and R^7 are hydrogen; G_m is $-NR^3CO-$ in either orientation; R^3 is hydrogen; D and D_m are $(CR^6R^7)_z$; y is 1; z is 2; each pair of A-A_m and B-

B_m are >N-C(O)-CH_2- ; I is -NR^8R^9 or -$NR^{10}C(O)R^{11}$ where R^8, R^9, R^{10} and R^{11} independently are hydrogen, alkyl, an amino protecting group, a reporter ligand, an intercalator, a chelator, a peptide, a protein, a carbohydrate, a lipid, a steroid, a nucleoside, a nucleotide, a nucleotide diphosphate, a nucleotide triphosphate, an oligonucleotide, an oligonucleoside, a soluble polymer, a non-soluble polymer, a reporter enzyme, a reporter molecule, a terpene, a phospholipid, a cell receptor binding molecule, a water soluble vitamin, a lipid soluble vitamin, an RNA/DNA cleaving complex, a porphyrin, or a polymeric compound selected from polymeric amines, polymeric glycols and polyethers; and Q is -CO_2H, -CO_2R^8, or -$CONR^8R^9$ (see page 6, line 9 to page 10, line 20). In some embodiments, R^8, R^9, R^{10} and R^{11} independently are hydrogen, alkyl, a peptide, a protein, a carbohydrate, a nucleoside, a nucleotide, a nucleotide diphosphate, a nucleotide triphosphate, an oligonucleotide, or an oligonucleoside (see page 10, lines 5-9) In other embodiments, R^8, R^9, R^{10} and R^{11} independently are a nucleoside, a nucleotide, an oligonucleotide, or an oligonucleoside (*Id.*).

6. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

This appeal seeks to resolve whether or not the Examiner has demonstrated, in accordance with the judicially-created doctrine of obviousness-type double patenting, that those of ordinary skill in the art would have regarded the subject matter claimed in claims 53, and 63 as an obvious variant of the subject matter claimed in claims 1 and 12 of U.S. Patent 6,613,873.

7. Grouping of the Claims

Claims 53 and 63 stand or fall together. Claim 64 is not subject to the appealed rejection based on claims 1 and 12 of U.S. Patent 6,613,873.

8. ARGUMENT

The Rejection Of Claims 53 and 63 Under The Judicially-Created Doctrine Of Obviousness-Type Double Patenting Based On Claims 1 and 12 Of U.S. Patent 6,613,873 Is Improper.

The doctrine of double patenting is designed to prevent the unjustified extension of patent exclusivity beyond the term of a patent. MPEP § 804. Nonstatutory-type double

patenting rejections are based on a judicially created doctrine grounded in public policy primarily intended to prevent prolongation of the patent term by prohibiting claims in a second patent which are not patentably distinct from claims in a first patent. *Id.*; *Eli Lilly & Co. v. Barr Labs, Inc.*, 222 F.3d 973 (Fed. Cir. 2000); *In re Braat*, 937 F.2d 589, 592 (Fed. Cir. 1991); *In re Longi*, 759 F.2d 887 (Fed. Cir. 1985) (explaining that, even though no explicit statutory basis exists for obviousness-type double patenting, the doctrine is necessary to prevent a patent term extension through claims in a second patent that are not patentably distinct from those in the first patent).

Although the Examiner asserts that there is overlap among the claims (September 16, 2005 Advisory Action at page 2), no such overlap actually exists. Claims 1 and 12 of the 873 patent require that at least one L be a 2,6-diaminopurine nucleobase. In the instant claims, each L is a naturally occurring nucleobase.

As is well known, the analytic approach employed in connection with an obviousness-type double patenting determination parallels that employed in connection with a 35 U.S.C. § 103 obviousness determination. *In re Braat*, 19 U.S.P.Q.2d 1289 (Fed. Cir. 1991). Thus, even if there were overlap between the instant claims and those of the 873 patent, the MPEP cautions that this still would provide inadequate support for an obviousness rejection. On this matter, the MPEP states "[t]he fact that a claimed species or subgenus is encompassed by a prior art genus is not sufficient by itself to establish a *prima facie* case of obviousness." MPEP § 2144.08, II. Rather, there must be a teaching that would have motivated one of ordinary skill in the art to make a claimed compound based on claims 1 and 12 of the 873 patent. *In re Fine*, 837 F.2d 1071, 1074, 5 U.S.P.Q.2D (BNA) 1596, 1598 (Fed. Cir. 1988) (obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art.).

The Examiner has failed to identify proper motivation to modify the compounds claimed in claims 1 and 12 of the 873 patent. Claims 1 and 12 of the 873 patent encompass numerous species. The amount of picking and choosing from the teachings of claims 1 and 12 of the 873 patent that would be required to arrive at any instant invention is inconsistent with obviousness. In the instant claims, L is a naturally occurring nucleobase while the 873 patent allows that L can also be non-naturally occurring nucleobases and at least one L has to be a 2,6-diaminopurine nucleobase—not a naturally occurring nucleobase. Claims 1 and 12

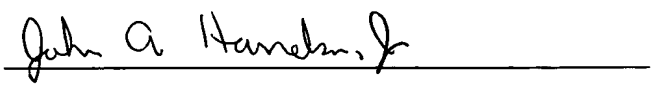
of the 873 patent also allow that $R^{7'}$ is H or C_1-C_8 alkylamine. In the instant claims, the corresponding variables R_6 and R_7 are each H. Applicants submit that these differences are significant, and that the instant claims are not obvious in view of the cited art.

The only motivation for modifying the teaching of the 873 patent that the Examiner has put forward is that genus of the cited art is so small as to make the compounds of the instant claims "immediately envisioned" (September 16, 2005 Advisory Action at page 2). This assertion is not consistent with the amount of picking and choosing needed to arrive at any claimed invention. Such picking and choosing, without any apparent motivation, is inconsistent with obviousness. Thus, Applicants submit that the rejection is improper.

9. CONCLUSION

For the foregoing reasons, Applicants request that this patent application be remanded to the Patent Office with an instruction to both withdraw the outstanding rejections and allow the appealed claims.

Respectfully submitted,



Date: October 4, 2005

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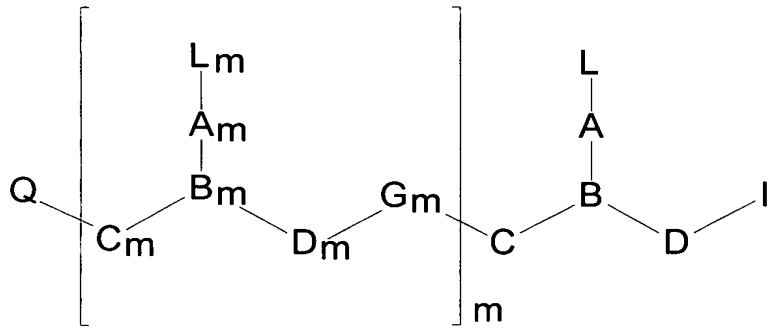
10. CLAIMS APPENDIX

1-52 (canceled)

53. (previously presented) A peptide nucleic acid of the formula:



wherein:

m is an integer from 1 to about 50;

L and L_m independently are naturally occurring nucleobases;

C and C_m are $(CR^6R^7)_y$; wherein:

R^6 and R^7 are hydrogen;

R^3 is hydrogen;

D and D_m are $(CR^6R^7)_z$;

y is 1 and z is 2;

G_m is $-NR^3CO-$ in either orientation;

each pair of A-A_m and B-B_m are $>N-C(O)-CH_2-$;

I is $-NR^8R^9$ or $-NR^{10}C(O)R^{11}$; wherein:

R^8, R^9, R^{10} and R^{11} independently are hydrogen, alkyl, an amino protecting group, a reporter ligand, an intercalator, a chelator, a peptide, a protein, a carbohydrate, a lipid, a steroid, a nucleoside, a nucleotide, a nucleotide diphosphate, a nucleotide triphosphate, an oligonucleotide, an oligonucleoside, a soluble polymer, a non-soluble polymer, a reporter enzyme, a reporter molecule, a terpene, a phospholipid, a cell receptor binding molecule, a water soluble vitamin, a lipid soluble vitamin, an RNA/DNA cleaving complex, a porphyrin, or a polymeric compound selected from polymeric amines, polymeric glycols and polyethers; and

Q is $-CO_2H$, $-CO_2R^8$, or $-CONR^8R^9$.

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APPEAL BRIEF TRANSMITTAL PURSUANT TO 37 CFR § 1.192

Transmitted herewith in triplicate is the APPEAL BRIEF in this application with respect to the Notice of Appeal received by The United States Patent and Trademark Office on **April 5, 2005**.

☐ Applicant(s) has previously claimed small entity status under 37 CFR § 1.27 .

☐ Applicant(s) by its/their undersigned attorney, claims small entity status under 37 CFR § 1.27 as:

- ☐ an Independent Inventor
- ☐ a Small Business Concern
- ☐ a Nonprofit Organization.

☒ Petition is hereby made under 37 CFR § 1.136(a) (fees: 37 CFR § 1.17(a)(1)-(4) to extend the time for response from the Notice of Appeal filed on April 5, 2005 to and through October 5, 2005 comprising an extension of the shortened statutory period of Four (04) month(s).

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	SMALL ENTITY		NOT SMALL ENTITY	
	RATE	FEE	RATE	FEE
☒ APPEAL BRIEF FEE	$250	$	$500	$500.00
☐ ONE MONTH EXTENSION OF TIME	$60	$	$120	$0.00
☐ TWO MONTH EXTENSION OF TIME	$225	$	$450	$0.00
☐ THREE MONTH EXTENSION OF TIME	$510	$	$1020	$0.00
☒ FOUR MONTH EXTENSION OF TIME	$795	$	$1590	$1,590.00
☐ FIVE MONTH EXTENSION OF TIME	$1080	$	$2160	$0.00
☐ LESS ANY EXTENSION FEE ALREADY PAID	minus	($)	minus	($0.00)
TOTAL FEE DUE		$		$2,090.00

☒ The Commissioner is hereby requested to grant an extension of time for the appropriate length of time, should one be necessary, in connection with this filing or any future filing submitted to the U.S. Patent and Trademark Office in the above-identified application during the pendency of this application. The Commissioner is further authorized to charge any fees related to any such extension of time to Deposit Account 23-3050. This sheet is provided in duplicate.

☒ A check in the amount of **$2,090.00** is attached. Please charge any deficiency or credit any overpayment to Deposit Account No. 23-3050.

☐ Please charge Deposit Account No. 23-3050 in the amount of **$ .00**. This sheet is attached in duplicate.

☒ The Commissioner is hereby authorized to charge any deficiency or credit any overpayment of the fees associated with this communication to Deposit Account No. 23-3050.

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